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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/887,505	07/02/1997	ROBERT L. KILKUSKIE	HYZ-040CIP	1117

7590 04/29/2005

HALE AND DORR
60 STATE STREET
BOSTON, MA 02109

EXAMINER	
MARTINELL, JAMES	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 04/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/887,505	KILKUSKIE ET AL.	
	Examiner	Art Unit	
	James Martinell	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31 and 42-46* is/are pending in the application.

4a) Of the above claim(s) *7,23,24,26,29,31 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-22,25,27,28,30 and 42-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 July 1997* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/6/04&3/5/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Appendix A*.

The requirement for restriction mailed July 1, 2004 is vacated and is replaced by the requirement for restriction below.

Claims 1-31 and 42-46 are drawn to oligonucleotides, modified oligonucleotides, and pharmaceutical compositions containing oligonucleotides or modified oligonucleotides.

Claims 1-31 are drawn to nucleotides, nucleotide constructs, and/or methods requiring the use of nucleotides or nucleotide constructs that contain more than one individual, independent, and distinct nucleotide sequence in alternative form. Accordingly, these claims are subject to restriction under 35 U.S.C. § 121 as outlined in 1192 O.G. 68 (November 19, 1996). This notice permits the examination of from one to ten independent and distinct nucleotide sequences in a single application based upon USPTO resources. The USPTO frequently restricts examination to one elected sequence. Since applicants have already elected two sequences, the claims including those sequences are examined on the merits. This requirement for election of SEQ ID NOs is not a requirement for an election of species, but a requirement for election of a single invention.

Claims 42-45 are drawn to compositions reciting different combinations of individual nucleotide sequences. Applicant is required to select one combination for examination. If the selected combination contains ten or fewer sequences, all of the sequences of the combination will be searched. If the selected combination contains more than ten sequences, the combination will be searched until one nucleotide sequence is found to be allowable. The order of searching will be chosen by the examiner to maximize the identification of an allowable sequence. If no individual nucleotide sequence is found to be allowable, the examiner will consider whether the combination of sequences taken as a whole renders the claims allowable. The identification of any allowable sequence(s) will cause all combinations containing the allowed sequence(s) to be allowed. See O.G. 68 (November 19, 1996) and MPEP 803.04.

Since applicants have already elected two sequences for examination (*viz.* SEQ ID NOs: 28 and 38), all of the claims that are drawn to either one of those sequences will be examined on the merits. Likewise, the combination claims 42-45 will be examined insofar as the combinations therein contain at least one of SEQ ID NOs: 28 or 38. It is further noted that SEQ ID NOs: 119-130 are the same as SEQ

ID NO: 28 (some of the SEQ ID NOs: 119-130 being RNA sequences). Accordingly, claim 21 is also examined on the merits.

Since this requirement for restriction is not final, applicants have the right to traverse in their next response.

Claims 7, 23, 24, 26, 29, 31, and 46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The references crossed out on form PTO-1499 submitted February 6, 2004 were already of record.

The disclosure is objected to because of the following informalities.

(a) The address for the ATCC (page 70, line 12) is incorrect. The current address for the ATCC should be substituted.

Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8-22, 25, 27, 28, 30, and 42-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are vague, indefinite, incomplete, inaccurate, and misdescriptive.

(a) Claims 1, 22, and 42-45 are vague and indefinite because they claim more than was elected.

(b) The recitation of "synthetic oligonucleotide" (claims 1, 2, 4, 5, 8, 43) is vague and indefinite because the instant application does not distinguish between synthetic oligonucleotides and non-synthetic oligonucleotides.

(c) Claims 1, 21, and 22 are incomplete because they refer to tables in the specification. There is no provision for referring to tables in the claims.

(d) The recitation of "the 5' untranslated region" (claims 4 and 5) is incomplete because there is no antecedent basis for the phrase.

(e) Claim 21 is inaccurate and misdescriptive because the sequences listed in the claim are not complementary to two or more non-contiguous regions of the HCV genome or HCV messenger RNA (see claim 2 from which claim 21 depends). Each of the sequences mentioned in claim 21 is the same as SEQ ID NO: 28 (see claim 1). The definition at page 11, first full paragraph of the application indicates that non-contiguous complementary regions hybridize under physiological conditions.

(f) The recitation of "self stabilized by a loop" (claim 25) is vague and indefinite because the phrase is not a structural property of the molecule, but depends upon the conditions in which the molecule finds itself. The "loop" may form or not form under a variety of conditions. The conditions are not described with clarity. Thus, the metes and bounds of the claim are not clear.

(g) The recitation of "the molecule" (claim 27) is incomplete because there is no antecedent basis for the term.

(h) The recitation of "at least one additional triplex-forming strand" (claim 30) is incomplete because there is no antecedent basis for the phrase.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-6, 8-20, 25, 27, 28, 30, 43, and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant application does not provide an adequate written description of all of the possible oligonucleotides that are embraced by the claims. The instant application does not provide a written description of all of the functional regions listed in the claims (*e.g.*, see claims 4 and 5).

Claims 2-6, 8-20, 25, 27, 28, 30, 43, and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO: 38, does not reasonably provide enablement for all of the claimed combinations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The discussion in the previous rejection is incorporated here.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8, and 12 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Sheridan et al (WO 93/13224 (July 8, 1993)). Sheridan et al discloses an oligonucleotide of 33 nucleotides length that includes the 20 nucleotides of SEQ ID NO: 28. Compare sequence HCV.33.8 in Figure 3.1, nucleotides 10-29 of Sheridan et al to SEQ ID NO: 28 of the instant application and see Appendix A attached to this Office action.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13-21, 25, 27, 28, 30, 42, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheridan et al (WO 93/13224 (July 8, 1993)) in view of applicants' admitted state of the prior art (*e.g.*, instant application at page 16, line 19 through page 19, line 29). Sheridan et al discloses an oligonucleotide of 33 nucleotides length that includes the 20 nucleotides of SEQ ID NO: 28. Compare sequence HCV.33.8 in Figure 3.1, nucleotides 10-29 of Sheridan et al to SEQ ID NO: 28 of the instant application and see Appendix A attached to this Office action. Applicants acknowledge the use of oligonucleotides as antisense agents to be old and also acknowledge the modification of oligonucleotides in antisense oligonucleotides to be old (instant application, page 16, line 19 through page 19, line 29). It would have been obvious for one of ordinary skill in the art at the time the invention was made to use the oligonucleotide of Sheridan et al as an antisense agent and further to modify moieties within the oligonucleotide to improve its use as an antisense agent as admitted to be old by applicants.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James Martinell whose telephone number is (571) 272-0719. The fax phone number for Examiner Martinell's desktop workstation is (571) 273-0719. Only documents such as those intended for use in a personal or telephone interview should be faxed to the examiner's desktop workstation. Any Official Communication to the USPTO should be faxed to (571) 273-8300.

The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be e-mailed to james.martinell@uspto.gov. Since e-mail communications may not be secure, it is suggested that information in such requests be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745.

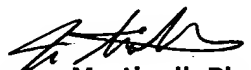
OFFICIAL FAX NUMBER

The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300. Any Official Communication to the USPTO should be faxed to this number.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



James Martinell, Ph.D.
Primary Examiner
Art Unit 1634

4/28/05

Appendix A 1/1

```
XX
PR   08-MAY-1991;   91US-00697326.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Cha T,  Beall E,  Irvine B,  Kolberg J,  Urdea MS;
XX
DR   WPI; 1992-398869/48.
XX
PT   Compsn. comprising a non-hepatitis C virus-1 nucleotide sequence -
PT   related to HCV-1, useful for treating and detecting HCV-1 infections and
PT   as a vaccine.
XX
PS   Claim 63; Page 140; 186pp; English.
XX
CC   A sandwich hybridisation assay can be used for HCV-1 genotyping analysis.
CC   One example uses nucleotide sequences which correspond to sequences in
CC   the C gene and the 5' UT region of HCV isolates as either capture or
CC   detection probes. Probe 126 is preferably used as a labelled probe.
CC   (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 33 BP; 8 A; 13 C; 6 G; 6 T; 0 U; 0 Other;

  Query Match             100.0%;  Score 20;  DB 2;  Length 33;
  Best Local Similarity   100.0%;  Pred. No. 0.06;
  Matches   20;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 TTCGCGACCCAACACTACTC 20
              ||||||||||||||||||||
Db         10 TTCGCGACCCAACACTACTC 29


RESULT 47
AAQ46463
ID   AAQ46463 standard; DNA; 33 BP.
XX
AC   AAQ46463;
XX
DT   25-MAR-2003  (revised)
DT   13-DEC-1993  (first entry)
XX
DE   Hepatitis C virus RNA assay label probe HCV.33.8.
XX
KW   Detection; HCV; reduced background signal; improved reproducibility;
KW   hybridisation; 5'-untranslated region; C gene; ss.
XX
OS   Synthetic.
XX
PN   WO9313224-A1.
XX
PD   08-JUL-1993.
XX
PF   22-DEC-1992;   92WO-US011343.
XX
PR   23-DEC-1991;   91US-00813338.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Sheridan P,  Chang C,  Running J;
XX
DR   WPI; 1993-227338/28.
XX
PT   Immobilising nucleic acid probe on styrene!, useful for HCV sequence
PT   detection - by using intermediate passively adsorbed polymer having
PT   functional gps. for covalently bonding to probe via its base-stable
PT   linkages.
XX
PS   Example; Fig 3.1; 34pp; English.
XX
CC   The sequence is that of a synthetic label probe which is complementary to
CC   nucleotide sequences in the hepatitis C virus C gene and the 5'-
CC   untranslated region. It may be used in an assay for the detection of HCV
CC   RNA. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 33 BP; 8 A; 13 C; 6 G; 6 T; 0 U; 0 Other;

  Query Match             100.0%;  Score 20;  DB 2;  Length 33;
  Best Local Similarity   100.0%;  Pred. No. 0.06;
  Matches   20;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 TTCGCGACCCAACACTACTC 20
              ||||||||||||||||||||
Db         10 TTCGCGACCCAACACTACTC 29


RESULT 48
AAV07837
ID   AAV07837 standard; DNA; 33 BP.
XX
AC   AAV07837;
XX
DT   27-AUG-2003  (revised)
DT   25-MAR-2003  (revised)
DT   10-DEC-1998  (first entry)
XX
DE   HCV.33.8 amplifier probe.
XX
KW   Comb-type branched polynucleotide; amplification multimer; analyte;
KW   hybridisation assay; hepatitis c virus; HCV; amplifier probe; ss.
XX
OS   Synthetic.
OS   Hepatitis C virus.
XX
PN   US5710264-A.
XX
PD   20-JAN-1998.
XX
PF   07-JUN-1995;   95US-00478085.
XX
PR   27-JUL-1990;   90US-00558897.
PR   23-DEC-1991;   91US-00813588.
XX
PA   (CHIR ) CHIRON CORP.
XX
PI   Chang C,  Fultz TJ,  Warner B,  Urdea MS,  Horn T;
XX
DR   WPI; 1998-109872/10.
XX
PT   New large comb-type branched polynucleotides - useful as amplification
PT   multimers in nucleic acid hybridisation assays.
XX
PS   Example 6; Col 25; 33pp; English.
XX
CC   The invention relates to a large comb-type branched polynucleotide of
CC   formula: 3'-A-S-(S'-X')m-S''-5'; where X' is a branched site joined to -
CC   (R)n-S'''-E-L; A = an oligonucleotide complementary to an analyte nucleic
CC   acid sequence; S = a first spacer segment of 1-50 linked monomers where
CC   each monomer is selected from nucleotides and a cleavable linker R; S' =
CC   a branching site spacer segment of 0-15 linked monomers where each of the
CC   monomers is selected from nucleotides and cleavable linker R; X' = a
CC   multifunctional nucleotide that provides a branch site; m = 1-100; S'' =
CC   a second spacer segment of 0-10 linked monomers where each of the
CC   monomers is selected from nucleotides and cleavable linker R; R = a
CC   cleavable linker molecule; n = 0 or 1; S''' = a third spacer segment of 0
CC   -10 linked monomers where each of the monomers is selected from
CC   nucleotides and cleavable linker R; E = an oligonucleotide segment of 5-
CC   10 nucleotides; L = an oligonucleotide containing 2-10 iterations of a
CC   nucleotide sequence complementary to a labelled nucleic acid probe. The
CC   invention also relates to a branched nucleic acid polymer. The poly-
CC   nucleotides are useful as amplification multimers in nucleic acid
CC   hybridisation assays used for genetic research, biomedical research and
CC   clinical diagnostics. Since the polynucleotide multimers include a large
CC   number (at least 20) iterations of a sequence that are available for
CC   specific hybridisation, they permit a greater degree of amplification and
CC   decrease the threshold level of a detectable analyte. The present
CC   sequence represents a hepatitis c virus (HCV) amplifier probe. (Updated
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